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EXAMINER	
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ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/588,859	KATO ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *1 and 2* is/are allowed.

6)☐ Claim(s) *3-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/9/06, 11/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-13, are pending in this application.

Rejoinder

Non-elected claims 12-13, are rejoined. The restriction of the claims is now withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims lack adequate support in the specification. Claims 3-8, 10, are drawn to inhibition of cytokine production, treatment of all disorders accompanied by hyperactive immune functions or systemic organ diseases. These are not practical utilities under the US patent practice. To ascertain the utilities, one must read the specification into the claims contrary to several precedent decisions by the US courts and Official practice. Even then, the claims would become duplicates of 9 and 11. The claims are attempts by applicant to claim prevention/treatment of all diseases known today and that may be discovered in the future, arising from cytokine production or hyperactive immune functions. They are reach-through claims and are no longer patentable under the US patent practice. Also, duplicates or substantial duplicate claims cannot be in the same application under the US patent practice. A claim must stand alone to define the invention, and incorporation into the claims by reference to the specification or an external source is not permitted. Ex parte Fressola, 27 USPQ 2d 1608,

BdPatApp & Inter. (1993). In patent examination, it is essential for claims to be precise, clear, correct, and unambiguous. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). By deleting the claims the rejection would be overcome.

Claims 3-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the claimed mechanisms and the diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

"'In the context of determining whether sufficient "utility as a drug, medicant, and the like in human therapy" has been alleged, It is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the [compounds and the utilities] as obviously correct." *In re Jolles*, 628 F.2d 1327, 1332 (Fed. Cir. 1980), citing *In re Novak*, 306 F.2d 924 (CCPA 1962); see 340 F.2d 974, 977-78 (CCPA 1965).

"A specification disclosure which contains a teaching of the manner and process of making and using the invention . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), Id. at 1566, quoting *Marzocchi*, 439 F.2d 220, 223 (CCPA 1971); *Fiers v. Revel,* 984 F.2d 1164, 1171-72 (Fed. Cir. 1993), quoting *Marzocchi*, 439 F.2d at 223; see also *Armbruster*, 512 F.2d 676, 677 (CCPA 1975); *Knowlton*, 500 F.2d 566, 571 (CCPA 1974); *Bowen*, 492 F.2d 859 (CCPA 1974); *Hawkins*, 486 F.2d 569, 576 (CCPA 1973).

Where there is "no indication that one skilled in the art would accept without question [the instant compounds and method of use] and no evidence has been presented to demonstrate that the claimed products do have those effects *Novak*, 306 F.2d at 928, an

applicant has failed to sufficiently demonstrate sufficient utility and therefore cannot establish enablement.'" *In re Rasmusson,* 75 USPQ2d 1297 (CAFC 2005). The claimed invention is not enabled without undue experimentation for the following reasons:

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered. *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC, 1988): "The factors to be considered [in making an enablement rejection] have been summarized as a) the breadth of the claims, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and, the quantity of experimentation necessary, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex prate Formal*, 230 USPQ 546. The breadth of the claims includes many compounds. The compounds embraced by the claims are numerous and are in the thousands. The nature of the invention is using the compounds as pharmaceuticals. There is no known prior art that broadly teaches treatment of all disorders arising from cytokine production, hyperactive immune functions or systemic autoimmune diseases.

The specification fails to set forth how one of ordinary skill in the art would identify "normal" patients who would have increased cytokine production in the future, and how such could be treated so as to prevent the occurrence or increase cytokine production or the diseases listed in claims 9 and 11. Given no guidance in the specification one of ordinary skill in the art would have to perform significant amount of experiments to make and use the invention as claimed.

It is quite possible that a mutation in the gene for the protein responsible for cytokine production may lead to increase/decrease production. To use the invention as claimed, one of ordinary skill in the art would have to perform experimentation in every instance to determine if

there is increased or decreased cytokine production and if such is due to genetic mutation in a patient or not. After prospective patients are identified and treated, assays must be performed on each one to determine if treatment is successful. However, the specification fails to disclose a routine procedure to perform such assays. Therefore, to make and use the instant invention, one of ordinary skill in the art would have to perform significant amount of experimentations. Such is deemed undue experiment under the US patent practice.

The specification listed diseases for which the instant compounds are applicable on pages 2-3. However, such are deemed speculations because there is no conclusive evidence that the compounds are applicable to the claimed diseases. There are no assays establishing correlation between the assays and each disease in claims 9 and 11. Applicant must provide evidence of correlation between cytokine inhibition and each disease listed in claims 9 and 11 through biological assays or published journals showing such assays.

Inflammation is a secondary response in many diseases including cancers, tumors, accident victims, etc. No evidence in the specification that cytokine production or eosinophiles are involved in each disease listed in claims 9 and 11.

Type I diabetes, claim 11, is a genetic disease treatable by insulin injection. No evidence in the instant specification or prior arts supports the disease as immune reaction. This is true for several diseases in claims 9 and 11. For example, multiple sclerosis, etc.

Above enumerated uncertainties present one of ordinary skill in the art with obstacles and prevents her from accepting the claimed therapeutic regimen on its face. The level of ordinary skill in the art of pharmaceutical art is high. The level of unpredictability in pharmaceutical art is very high. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is

generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

There are no disclosures in the specification establishing a link between the activities of the instant compounds and each of the claimed diseases. There is no absolute predictability or established correlation between the claims and the specification disclosures. Predictability in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. In the instant invention, there is no direction or guidance by applicant because assays are not performed for establishing nexus between the assays' results and specific disorders. The specification fails to cite references disclosing conclusive evidence of relationships between the mechanisms and all the claimed disorders. Therefore, there is no evidence in the specification that established correlation between the disclosure and the instantly claimed invention. *See Ex parte Mass*, 9 USPQ2d 1746, (1987).

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding any of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. By deleting the claims the rejection would be overcome.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 3-13, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For the reasons set forth above under 35 USC 112, first paragraph the claims are indefinite. See the Examiner's suggestions above.

Claims 3-7 improperly depend from 1 for failure to limit the scope of 1. The claims are drawn to the same compounds as claim 1 but recite mechanism of action of the compounds. Mechanisms of actions (intended use) of the compounds are inherent in claim 1. Also, intended use is not a limitation of a compound or product. *In re Hack*, 114USPQ 161 (CCPA, 1957); In *re Craig*, 90 USPQ 33 (CCPA, 1951); *In re Brenner*, 82 USPQ 49 (CCPA, 1949).

The term "comprising" in claim 3 renders 3-7 indefinite. The claims are drawn to compounds. A compound can only consist of itself.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujii et al., US 5,977,410.

Applicant claims process of making compounds of claim 1 comprising reacting formula II with formula III or thiolation of compounds of formula IV with a thiocarbonylating agent.

Determination of the scope and content of the prior art (MPEP 2141.01)

Fujii et al., teach a similar process comprising reacting formula 2 with formula 3 (col. 5, line 50 to col. 6, line 12; col. 10, line 3 to col. 11, line 3) or thiolation of compounds of formula Ia with a sulfurizing (thiocarbonylating) agent (col. 14, line 50 to col. 15, line 33). Fujii et al., also teach the compounds wherein A is S or O, and their process is applicable in either case.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the instant invention and that of Fujii et al., are the substituents of the starting reagents.

Finding of prima facie obviousness---rational and motivation (MPEP 2142.2413)

The instant starting materials and that of the prior art are analogous starting compounds because the processes involve the reaction of the same elements in the starting materials: between a leaving group (in formula II/2) and amine (in formula III/3) or replacement of O with S in formula IV/Ia. There is no evidence in the specification or the prior art that other substituents of the starting materials are involved in the reactions. The use of analogous material in a well known process is prima facie obvious. *In re Durden,* 226 USPQ 359 (1985). See also *In re Farkas,* 152 USPQ 109 (1966). "Employing a different starting material in a generally old reaction is prima facie obvious. Applicant must show evidence reaction would not be expected to take place or that the starting materials would behave in a manner different from those of the reference."

Therefore, the instant invention is prima facie obvious from the teaching of Fujii et al. One of ordinary skill in the art would have known to use the process of Fujii et al., in making compounds of formula I at the time the invention was made. The motivation is from the teachings of the prior art.

Alternatively, given the teachings of the prior art, it would have been obvious for one of ordinary skill in the art faced with the need to make compounds of formula I, to try the reaction of a leaving group in formula II/2 with amine in formula III/3 or replace O with S in formula IV/Ia at the time the invention was made.

When there is motivation

> to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a

combination was obvious to try might show that it was obvious under [35 USC] 103.

KSR Int'l Co. v. Teleflex Inc., 127 S.Ct 1727, 82 USPQ2d 1385, 1397 (2007).

Allowable Claims

Claims 1-2 are allowable over prior arts of record.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

/Taofiq A. Solola/

Primary Examiner, Art Unit 1625

March 10, 2009